VESIcare® solifenacin succinate: Preferred Drug List Overview of New Clinical Studies

This information is provided in response to an unsolicited request.

Patients with overactive bladder (OAB) experience urgency, urge incontinence and a frequent need to urinate, symptoms which adversely affect quality of life and overall health. VESIcare has previously been shown to significantly reduce episodes of frequency, urgency and urge incontinence, while increasing warning time. Together, these improve patient quality of life and sense of control. Recent studies have shown that solifenacin can:

- improve residual urgency symptoms in patients previously treated with tolterodine ER 4 mg;
- improve patient-reported outcomes for OAB symptoms across several domains;
- be effective in reducing the frequency of OAB symptoms after 1 week of treatment; and
- reduce the frequency of severe urgency episodes.

New clinical efficacy data:

1. In the VERSUS trial (12 weeks, open-label, flexible dose 5 or 10 mg), the efficacy of VESIcare was studied in patients who had been treated with tolterodine ER 4 mg for ≥4 weeks and still experienced residual urgency symptoms (defined as more than 3 urgency episodes per 24 hr). Data were collected at pre-washout, post-washout, 1 week, 4, 8 and 12 weeks.[1]
   a. After a 14-day washout period, VESIcare significantly reduced the number of daily urgency episodes (median percent reduction of 75% from pre-washout to end of study).
   b. VESIcare significantly improved diary variables (micturitions, incontinence episodes, nocturia episodes, nocturnal voids) and OAB-q scales and domains compared to pre- and post-washout.
   c. Treatment-emergent adverse events included dry mouth (17.5%), constipation (11.6%), blurred vision (2.3%) and headache (2.9%), and at rates similar to that reported in previous trials.
2. The SUNRISE trial (randomized, double-blind, 16-week, placebo-controlled, flexible dose 5 or 10 mg) reported that VESIcare was effective in reducing the mean number of *severe* urgency episodes with or without incontinence (the primary endpoint), which were defined by Patient Perception of Intensity of Urgency Scale of 3+4 in 3-day diaries.[2]
   a. The median reduction from baseline in the number of *severe* urgency episodes was 70% with VESIcare versus 50% with placebo.
   b. VESIcare significantly reduced micturition frequency, incontinence episodes and urgency incontinence episodes after 1 week of treatment.
   c. Treatment-emergent adverse events for VESIcare (5 or 10 mg) vs. placebo included dry mouth (15.8% vs. 2.7%), constipation (6.9% vs. 2.2%), and blurred vision (0.8% vs. 0.9%), and occurred at rates similar to that reported in previous trials.
   d. The significant improvements in urgency are consistent with those reported in the 2008 VENUS trial.
3. In the VIBRANT trial (12 week, randomized, double-blind, placebo-controlled, flexible dose 5 or 10 mg) VESIcare significantly improved patient reported outcomes from OAB and Health Related Quality of Life (HRQL) assessments and reduced urgency, urge incontinence, and frequency compared to placebo.[3]
   a. VESIcare significantly improved OAB-q Symptom Bother scores, HRQL overall scores and domain scores as compared to placebo.
   b. Significantly more VESIcare-treated patients reported treatment benefit (84% vs 63%), and willingness to continue (79% vs 60%; all Ps<0.0001).
   c. Treatment-emergent adverse events for VESIcare (5 or 10 mg) vs. placebo included: dry mouth (13.2% vs. 2.4%), constipation (8% vs 1.8%), dry eye (1.6% vs. 0.3% placebo) and blurred vision (1.0% vs. 1.3%).
4. A post-hoc analysis of over 2,225 subjects in VOLT (12 week, flexible dose VESIcare Open-Label Trial) stratified patient-reported outcomes by their most bothersome symptom, which included frequency, urgency, urge incontinence and nocturia. Statistical analysis was descriptive.[4]
   a. By study end, patient-reported outcomes stratified by their most bothersome symptom improved by 43.9% (nocturia), 51.7% (urge incontinence), 44.5% (urgency), and 46.3% (frequency).
   b. Treatment-emergent adverse events varied according to most bothersome symptom, and included dry mouth (17.9-27.7%), constipation (12.4-14.6%), and blurred vision (2.1-3.4%).

New clinical safety and tolerability data:

1. The VECTOR study (randomized, double-blind, double-dummy, 8 week trial with 132 patients) compared the tolerability (primary) and efficacy (secondary) of 5 mg VESIcare and 5 mg oxybutynin IR three times daily.[5]
   a. Both VESIcare and oxybutynin IR significantly reduced OAB symptoms and improved patient-reported outcomes.

   b. VESIcare treatment was associated with significantly fewer dry mouth episodes and significantly less dry mouth severity, as compared to oxybutynin IR. VESIcare was also associated with lower rates of adverse events and lower severity overall.
2. A recent study (12 week, open-label, post-marketing surveillance study) evaluated the effect of VESIcare on cardiovascular tolerability during routine use in 3,222 OAB patients.[6]
   a. No clinically meaningful alterations in mean heart rate (75.2 ± 8.2 beats/min pre-treatment vs 74.5 ± 7.6 beats/min at study end) were observed.
   b. No clinically meaningful alterations in mean blood pressure (137/82 mmHg pretreatment vs 134/81 mmHg at study end) were observed.
   c. In this study, age greater than 80 years and co-medications significantly affected adverse event incidence.

Important information from the package insert:

1. VESIcare (solifenacin succinate) tablets are indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency.
2. The recommended dose of VESIcare is 5 mg once daily. If the 5mg dose is well tolerated, the dose may be increased to 10 mg once daily.

Safety

1. The most common adverse events reported in patients treated with VESIcare were dry mouth (10.9%-5mg; 27.6%-10mg; 4.2%-placebo), constipation (5.4%-5mg; 13.4%-10mg, 2.9%-placebo), and blurred vision (3.8%-5mg; 4.8%-10mg; 1.8%-placebo).
2. VESIcare is contraindicated in patients with urinary retention, gastric retention, uncontrolled narrow-angle glaucoma, and in patients who have demonstrated hypersensitivity to the drug substance or other components of the product.
3. VESIcare, like other anticholinergic drugs, should be administered with caution to patients with clinically significant bladder outflow obstruction because of risk of urinary retention. VESIcare, like other anticholinergics, should be used in caution with decreased gastrointestinal motility. VESIcare should be used with caution in patients being treated for narrow-angle glaucoma. VESIcare should be used in caution in patients with reduced renal function. Doses of VESIcare greater than 5 mg are not recommended in patients with severe renal impairment (CLcr < 30 mL/min). VESIcare should be used with caution in patients with reduced hepatic function. Doses of VESIcare greater than 5 mg are not recommended in patients with moderate hepatic impairment (Child-Pugh B). VESIcare is not recommended for patients with severe hepatic impairment (Child-Pugh C). Do not exceed a 5 mg daily dose of VESIcare when administered with therapeutic doses of ketoconazole or other potent CYP3A4 inhibitors.
4. In terms of QTc information, no clinically relevant changes were seen for VESIcare 10 mg vs. placebo. This observation should be considered in clinical decisions to prescribe VESIcare for patients with a known history of QT prolongation or patients who are taking medications known to prolong the QT interval.

References

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